

## Role of tranexamic acid in reducing perioperative blood loss in transthoracic esophagectomy

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### Abstract

**Background and objectives:** Transthoracic esophagectomy is usually associated with significant perioperative bleeding and blood loss. The present study investigated the role of prophylactic tranexamic acid on intra- and postoperative blood loss and the need for blood transfusion in transthoracic esophagectomy (Ivor Lewis esophagectomy).

**Materials and Methods:** Patients who underwent laparotomy and right thoracotomy with intrathoracic anastomosis for esophageal malignancy were enrolled in the study. The enrolled cases were divided into two groups namely Group A and B. Informed consents were obtained from all the enrolled patients. Group A patients received a standard dose of 1 gram of intravenous tranexamic acid one hour before the beginning of surgery while Group B patients did not receive any tranexamic acid before or after the surgery. Perioperative blood loss was estimated and noted. Post-operative blood loss was assessed from the surgical drains.

**Results:** A total of 55 cases were included in the study. Group A and B had 27 and 28 cases respectively. The mean age of the Group A and Group B patients was  $60.1 \pm 6.2$  and  $60 \pm 6.9$  years respectively. Out of 27 cases in Group A, 7 (25%) patients had a postoperative haemorrhage (blood loss) up to 300 ml and among the remaining 20, only 2 (7%) patients required blood transfusion as hematocrit fell below 20%. Compared to Group A, patients in Group B who did not receive preoperative tranexamic acid, 21(75%) patients had postoperative haemorrhage up to 300 ml (Group A vs. Group B:  $p=0.0002$ ). Regarding intraoperative blood loss no significant ( $p > 0.05$ ) difference was observed among the cases in two groups.

**Conclusion:** The study revealed that administration of prophylactic tranexamic acid resulted into fewer postoperative blood loss in transthoracic esophagectomy.

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### Introduction

Esophageal cancer continues to represent a formidable challenge for both patients and clinicians. Surgical treatment remains a fundamental component of the treatment of localized esophageal carcinoma. Multiple approaches have been described for esophagectomy but the transthoracic approach is

widely practised [1,2]. The radical surgical procedures are associated with excessive perioperative blood loss and necessitate blood transfusion in the absence of blood conservation strategies. The intra-thoracic oesophagus lies in close vicinity to major vessels such as the aorta, azygous vein and pulmonary vessels and is supplied mainly by small branches from the aorta. The risk

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may be higher in patients with bulky esophageal tumors in close relation with the major vessels and in patients who have received preoperative chemotherapy or radiotherapy [3]. Surgery affects the coagulation systems and the fibrinolytic system shuts down due to increased release of plasminogen activator inhibitor [2].

Tranexamic acid is a synthetic lysine-analogue with anti-fibrinolytic activity that competitively inhibits the activation of plasminogen to plasmin, and is a well-documented blood sparing agent. Tranexamic acid has roughly eight times antifibrinolytic activity of an older analogue epsilon-aminocaproic acid [4]. The drug interfere with the formation of the fibrinolytic enzyme plasmin from its precursor plasminogen by plasminogen activators (primarily t-PA and u-PA) which takes place mainly in lysine rich areas on the surface of fibrin. The drug blocks the binding sites of the enzymes or plasminogen and thus stop plasmin formation.

The administration of tranexamic acid preoperatively significantly reduces blood loss in the first 24 hours in patients undergoing major surgeries for hip and femoral fractures as well it causes a significant reduction in postoperative anaemia and need for transfusion among these patients [5]. This would in turn, help avoid complications related to transfusion of blood and blood products. Also, preoperative administration of single bolus dose of tranexamic acid (20 mg/kg) significantly reduces blood loss in major surgeries of head and neck and other surgeries [6,7]. Thus, it reduces eventual need for blood transfusion. Tranexamic acid demonstrated a significantly lower risk of bleeding complications and transfusion requirements compared to placebo in patients undergoing coronary artery surgery without any significant increase in the risk of death or thrombotic complications [8]. A prospective double blind study reported that single intravenous bolus plus perioperative continuous infusion of tranexamic acid significantly reduce blood loss in abdominal oncosurgical procedures [9].

Transthoracic esophagectomy is a major surgery and hence there is always a significant risk of both intra- as well as postoperative bleeding and blood loss. There is a paucity of information on the efficacy of tranexamic acid in reducing the blood

loss in major surgery like transthoracic esophagectomy. With these considerations, we investigated the prophylactic role of tranexamic acid on the bleeding spectrum in transthoracic esophagectomy.

## Material and Methods

Patients with esophageal malignancy undergoing laparotomy and right thoracotomy with intrathoracic anastomosis (Ivor Lewis esophagectomy) for esophageal malignancy were enrolled in the study. The study was conducted from January 2018 to January 2020 at the Department of Cardiovascular and Thoracic Surgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. The study was approved by the institutional ethical board. Informed consent was obtained from all the cases prior to enrolment in the study.

The enrolled cases were divided into Group A and B. All the patients were of same race and were operated by the same team of surgeons. Group A patients received a standard dose of 1 gram of intravenous tranexamic acid one hour before the beginning of surgery while Group B patients did not receive any tranexamic acid before or after the surgery. Per-operative co-administration of procoagulant like fresh frozen plasma (FFP), platelet rich plasma (PRP), platelet concentrate (PC) was avoided. Patients having co-morbidities, any coagulation disorder or using any anticoagulants or antiplatelet drugs was not included in study.

The peroperative blood loss was estimated and noted. Postoperative blood loss was assessed from the surgical drains. The serial hematocrit and the need and number of postoperative blood transfusions were recorded in both the groups. The indication for transfusion in our study was based on intra-operative and post operative hematocrit value. Blood transfusion was given if the hematocrit value became less than 20%.

## Results

The mean age of Group A and B patients was  $60.1 \pm 6.2$  and  $60.0 \pm 6.9$  years respectively. In Group A, only 3 (11.1%) patients had an estimated intra-

**Table-1:** Comparison of perioperative blood loss in patients undergoing transthoracic esophagectomy with and without prophylactic tranexamic acid (N=55)

Parameter	Gr A (n=27) Number (%)	Gr B (n=28) Number (%)	P value**
<b>Intra-operative blood loss</b>			
200 ml	3 (11.1)	9 (32.1)	$p = 0.06$
< 200 ml	24 (88.9)	19 (67.9)	$p = 0.06$
<b>Post operative blood loss*</b>			
Up to 300 ml	7 (25.9)	21 (75)	$p = 0.0002$
<b>Hematocrit &lt;20%</b>	2 (7.4)	6 (21.4)	$p = 0.14$
<b>Blood transfusion</b>	2 (7.4)	6 (21.4)	$P = 0.14$

Note: Group A = received tranexamic acid; Group B = No tranexamic acid;

\*Assessed through surgical drain;\*\* p value calculated by Z test

operative blood loss of 200 ml while as remaining 24 (88.9%) patients had less than 200 ml intraoperative bleed compared to 9 (32.1%) and 19 (67.9%) cases respectively in Group B ( $p = 0.06$ ). After shifting to the ward, out of 27 cases in Group A, 7 (25%) patients had a postoperative bleeding up to 300 ml and among the remaining 20, only 2 (7%) patients required blood transfusion as hematocrit fell below 20%. Compared to Group A, patients in Group B who did not receive preoperative tranexamic acid, 21(75%) patients had postoperative haemorrhage up to 300 ml (Group A vs. Group B:  $p=0.0002$ ). No significant ( $p = 0.14$ ) differences were observed between the groups regarding the requirement for blood transfusion. Details are shown in Table-1.

## Discussion

For many years, tranexamic acid has been used in different types of surgical procedures to reduce blood loss during intra- and in post operative period to avoid eventual need for blood transfusion in surgical patients. Tranexamic acid has been extensively studied to reduce blood loss in orthopaedic [2,5], gynaecological [7,10], cardiac [8] and spine surgeries [8,11]. The treatment effect of tranexamic acid varies somewhat according to the type of surgery, but the result is overall beneficial in terms of reduction of blood loss during and after surgery. However, evidence-based studies regarding its optimal perioperative haemostatic

dose regimen in abdominal and abdomino-thoracic surgeries are still lacking. Different doses of the drug are being used in perioperative period which ranged from 10 mg/kg to 20 mg/kg, all showing variable effects on perioperative blood loss [9, 11]. In our study, in patients with transthoracic esophagectomy, significantly ( $p=0.0002$ ) fewer patients had post operative blood loss of up to 300ml with prophylactic tranexamic acid (1 gram) compared to the control group. However, there was no significant difference between the groups with regard to intra-operative blood loss and need for blood transfusion possibly could be due to low number of cases. Therefore, our encouraging result of low bleeding tendency during postoperative period is useful for preoperative prophylactic application of tranexamic acid in patients undergoing transthoracic esophagectomy. However due to small size of the study population, the validity of the efficacy of tranexamic acid in reducing perioperative blood loss in transthoracic esophagectomy needs further elaborative study.

**Conflict of interest:** None

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